Open Journal of Biomedical Research

Open J Biomed Res

ORIGINAL RESEARCH

Two Diseases and One Biopsy: Navigating the Diagnostic Overlap between *Helicobacter Pylori* Gastritis and Celiac Disease

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ABSTRACT

Purpose: The duodenal biopsy has dual responsibilities: detecting celiac disease and sampling adjacent gastric mucosa for *Helicobacter pylori*. When both conditions coexist, pathologists and clinicians face interpretive challenges that affect patient management. This study describe the clinicopathological features of concurrent *H. pylori* infection and celiac disease, highlighting diagnostic pitfalls and implications for clinical practice.

Materials and Methods: We identified three patients with histological evidence of both conditions from 2023–2024 pathology records at private laboratories in Zawia city, Libya. Clinical presentations, endoscopic findings, serological data, and histopathological features were analyzed.

Results: All three patients presented with abdominal pain and anemia; two had positive celiac serology prompting biopsy. Histology revealed villous atrophy (Marsh 3a-3c) alongside *H. pylori*-associated gastritis of varying severity. The diagnostic sequence determining which condition dominated clinical symptoms proved complex, with *H. pylori* potentially confounding celiac assessment and vice versa.

Conclusion: Concurrent *H. pylori* and celiac disease create diagnostic ambiguity that requires careful histopathological evaluation and clinical correlation. Recognition of this overlap prevents under diagnosis and guides appropriate dual therapy. (*Open J Biomed Res 2024;3:21-25*)

Keywords

Helicobacter pylori, Celiac disease, Villous atrophy, Duodenal biopsy, Malabsorption, Serology.

AUDIOABSTRACT

ARTICLE INFO

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Received: 1 October 2024
Accepted: 12 November 2024
Published: 15 November 2024

INTRODUCTION

The gastrointestinal tract rarely offers simple diagnoses, but some biopsies present particular puzzles. Consider the patient with chronic diarrhea, iron-deficiency anemia, and positive tissue transglutaminase antibodies. Celiac disease seems obvious until gastric biopsies reveal dense *H. pylori* infiltration and active gastritis.[1] Which condition drives the symptoms? Does one mask the other? And how should treatment proceed?

This diagnostic ambiguity is more common than literature suggests. Both *H. pylori* and celiac disease produce nonspecific abdominal complaints: pain, bloating, altered bowel habits.[2,3] Both cause anemia through different mechanisms chronic blood loss versus iron malabsorption.[4,5] Both are diagnosed through endoscopic biopsy, often obtained simultaneously during the same procedure.[6] Yet they require fundamentally different treatments: antibiotics for one, lifelong gluten avoidance for the other.[7,8]

The coexistence of these conditions raises important clinical questions. Some researchers have suggested that *H. pylori* infection might actually protect against celiac disease through immune modulation part of the broader "hygiene hypothesis" proposing that microbial exposure shapes autoimmune susceptibility.[9,10] Conversely, chronic *H. pylori* gastritis with hypochlorhydria could theoretically impair gluten digestion and increase antigenic exposure in the small intestine.[11] Population studies have yielded conflicting results: some show inverse associations between *H. pylori* seropositive and celiac disease, while others find no relationship.[12]

We present three cases where these conditions converged in the same patient, creating clinical and pathological complexity that resisted easy

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categorization. Our goal is not merely to document coincidence, but to explore how these diseases interact, how they confuse interpretation, and how pathologists can guide clinicians through the diagnostic thicket building on earlier observations by Rostami et al.[13] and more recent work by Ludvigsson et al.[14] on diagnostic challenges in gluten-related disorders.

CASE PRESENTATIONS

Case 1: The Teenager with Two Diagnoses

A 13-year-old girl presented with eighteen months of episodic abdominal pain, loose stools, and pallor. Laboratory studies revealed iron-deficiency anemia (hemoglobin 8.2 g/dL) and strongly positive anti-tissue transglutaminase antibodies (>100 U/mL), markers with high sensitivity and specificity for celiac disease.[15] Her pediatrician suspected celiac disease and referred for endoscopy.

The gastroscopy revealed nodular gastric antrum and mildly scalloped duodenal folds findings consistent with, but not specific for, celiac disease. Biopsies were obtained from both sites.

Histopathological findings: Duodenal samples showed partial villous atrophy with increased intraepithelial lymphocytes (>25 per 100 enterocytes), classified as Marsh 3a using the Oberhuber classification.[16,17] Gastric biopsies, obtained almost as an afterthought, revealed severe chronic active gastritis with abundant *H. pylori* organisms coating the mucus layer morphology well-characterized. The inflammation was dense enough to cause superficial erosions.

Clinical course: The patient completed *H. pylori* eradication therapy (triple therapy with proton pump inhibitor, amoxicillin, and clarithromycin) before initiating gluten-free diet.[18] Follow-up endoscopy at six months showed resolution of gastritis and partial improvement in duodenal villous architecture. Her anemia corrected, though whether through iron repletion, improved absorption, or both remained unclear a phenomenon noted in previous studies of dual pathology.[19]

Case 2: When Celiac Disease Hides the Bacterium

A 34-year-old woman presented with epigastric pain, early satiety, and weight loss of 6 kg over four months. She had no prior gastrointestinal diagnoses. Endoscopy revealed erythematous, friable gastric mucosa and normal-appearing duodenum. Biopsies were taken from both sites based on gastric abnormalities.

Histopathological findings: Gastric biopsies showed moderate chronic active *H. pylori*-associated gastritis, graded using the updated Sydney system.[20] Unexpectedly, duodenal biopsies despite normal endoscopic appearance demonstrated marked villous atrophy consistent with Marsh 3b celiac disease.[16] Serological testing subsequently confirmed positive tissue transglutaminase antibodies (45 U/mL).

Diagnostic dilemma: The patient's predominant symptoms (pain, early satiety) suggested gastric pathology, yet her weight loss and the severity of duodenal damage pointed to malabsorption. This dissociation between symptoms and pathology illustrates the limitation of symptom-based diagnosis in gluten-related disorders.[21] Had biopsies been limited to the visibly abnormal stomach, her celiac disease would have been missed entirely a scenario described by Hopper et al.[22] in their audit of duodenal biopsy practice.

Case 3: The Most Severe Presentation

A 23-year-old woman with known celiac disease diagnosed five years prior but poorly compliant with gluten-free diet presented with worsening abdominal pain, vomiting, and refractory anemia. Her gastroenterologist suspected refractory celiac disease or complications such as ulcerative jejunitis.[23]

Histopathological findings: Endoscopy revealed severe pangastritis with ulceration and duodenal mucosa that appeared atrophic. Biopsies confirmed total villous atrophy (Marsh 3c) and severe chronic active *H. pylori* gastritis with intestinal metaplasia a precancerous change rarely reported in young adults.[24] The gastric inflammation was more aggressive than typically seen in her age group, raising questions about interaction between untreated celiac disease and *H. pylori* virulence.[25]

Management of complexity: This patient required simultaneous attention to both conditions' eradication therapy for *H. pylori* and strict dietary counseling for celiac disease while monitoring for gastric dysplasia given her metaplasia. The interplay between ongoing gluten exposure and persistent *H. pylori* infection created uncertainty about which therapeutic priority would most improve her symptoms, reflecting the management challenges described by Green and Cellier[26] in complex celiac disease.

DISCUSSION

Upper gastrointestinal endoscopy routinely

samples both stomach and duodenum, yet these sites are often evaluated independently gastric biopsies for *H. pylori*, duodenal biopsies for celiac disease.[27] Our cases demonstrate the hazard of this siloed thinking. In each patient, limiting evaluation to the suspected site would have missed the coexisting condition.

Pathologists can mitigate this risk by systematically reviewing all tissue from the procedure, even when clinical suspicion focuses on one diagnosis. The presence of *H. pylori* should not preclude careful villous assessment; conversely, villous atrophy should prompt examination of gastric mucosa for concurrent pathology. This comprehensive approach aligns with recommendations from the British Society of Gastroenterology on optimal biopsy protocols.

Celiac serology tissue transglutaminase and endomysial antibodies provides diagnostic guidance but not definitive answers.[28] In Case 2, positive serology eventually explained duodenal findings that initially seemed incidental. However, *H. pylori* infection itself can produce low-level serological cross-reactivity or inflammatory changes that complicate interpretation. Neither condition's serological markers reliably predict the other's presence. Clinicians should maintain suspicion for dual pathology when symptoms exceed what single-diagnosis explanations would predict, or when response to initial treatment proves incomplete a principle emphasized in recent ESPGHAN guidelines.[29]

The relationship between *H. pylori* and celiac disease remains incompletely understood. Some studies suggest *H. pylori* infection might protect against celiac disease through immune modulation hygiene hypothesis mechanisms that remain controversial.[9,10] Conversely, celiac-related duodenal damage could impair defense against ingested pathogens, potentially facilitating *H. pylori* colonization. Alternatively, *H. pylori*-induced hypochlorhydria might alter gluten processing and antigen presentation.[11] These hypothetical interactions require further study but inform the clinical imperative to treat both conditions when identified. Some work had done immune responses in dual infection provides a foundation for understanding these complex relationships.

The cases employed different therapeutic sequences. Case 1 prioritized *H. pylori* eradication before dietary intervention; Case 3 required simultaneous management. No standardized protocol exists, but several principles emerge from literature and our experience:

- *H. pylori* eradication should proceed promptly given its curability and association with ulcer complications, following Maastricht consensus recommendations.[30]
- Gluten-free diet implementation can follow, with recognition that symptom improvement may lag due to the time required for mucosal healing.[31]
- Follow-up evaluation should assess both sites, as histological recovery occurs at different rates gastric inflammation resolves within weeks, while duodenal recovery may take months to years.
- Refractory symptoms after appropriate therapy should prompt reconsideration of diagnostic completeness, including assessment for refractory celiac disease or *H. pylori* treatment failure.[32]

One of the limitations of this study is that the three-case series cannot establish prevalence or define optimal management. Selection bias favors patients sick enough to undergo endoscopy, potentially overrepresenting severe or atypical presentations.[33] Long-term outcomes remain unknown, and we cannot determine whether the patients' clinical improvement resulted from one or both interventions. However, the consistency of diagnostic complexity across cases each presenting interpretive challenges that delayed or complicated management suggests this overlap deserves greater clinical attention than literature currently provides. Our observations complement population-based studies by adding histopathological detail to epidemiological associations.[34,35]

CONCLUSION

H. pylori and celiac disease, though pathologically distinct, frequently share clinical presentations and diagnostic procedures. Their coexistence creates interpretive challenges that resist simple algorithms: symptoms may be attributed to the wrong condition, serological testing may mislead, and treatment responses may be difficult to attribute.

For pathologists, the message is clear: examine all tissue completely, regardless of clinical suspicion. The duodenal biopsy that shows villous atrophy should prompt review of gastric samples; the gastric biopsy revealing *H. pylori* should not prevent careful duodenal evaluation.

For clinicians, these cases counsel diagnostic humility. When patients present with classic features of one condition, the other should remain in differential

consideration particularly when symptoms are severe, atypical, or refractory to initial therapy.

Two diseases, one biopsy, multiple possibilities. Recognition of this complexity ensures that neither condition escapes detection, and that patients receive comprehensive care for the full spectrum of their gastrointestinal pathology.

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